HFA-305

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

MAY 31 2002

Robert W. Pollock
Lachman Consultant Services, Inc.
1600 Stewart Avenue
Westbury, New York 11590

Re: Docket No. 01P-0356/CP1

Dear Mr. Pollock:

This responds to your citizen petition, dated August 15, 2001, requesting that the Commissioner of Food and Drugs amend the *Approved Drug Products with Therapeutic Equivalence Evaluations* (the Orange Book) to designate Cortef tablets (hydrocortisone), 5 milligrams (mg), 10 mg, and 20 mg (NDA 8-697) (a Pharmacia and Upjohn product) as a designated reference listed drug product for hydrocortisone tablets. Currently, Hydrocortone tablets (hydrocortisone), 20 mg (NDA 8-506) (a Merck product) is the reference listed drug product. For the reasons stated below, your petition is granted.

Section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)) allows the marketing of generic versions of previously approved drug products when the generic version is the subject of an approved abbreviated new drug application (ANDA). To gain approval, the ANDA must show, among other things, that the generic version has the same active ingredient in the same strength, that its labeling is essentially identical, and that it is bioequivalent to a listed drug (i.e., a previously approved drug product). The specific drug product to which an ANDA refers is the reference listed drug.

The Food and Drug Administration's (FDA's) policy on the designation of reference listed drugs is described in the preamble to the final rule establishing the requirements for ANDAs, published in the *Federal Register* of April 28, 1992 (57 FR 17950, 17958):

> . . . FDA will designate all reference listed drugs. Generally, the reference listed drug will be the NDA drug product for a single source drug product. For multiple source NDA drug products or multiple source drug products without an NDA, the reference listed drug generally will be the market leader as determined by FDA on the basis of commercial data. FDA recognizes that, for multiple source products, a product not designated as the listed drug and not shown bioequivalent to the listed drug may be shielded from direct generic competition. If an applicant believes that there are sound reasons for designating another drug as a reference listed drug, it should consult FDA.

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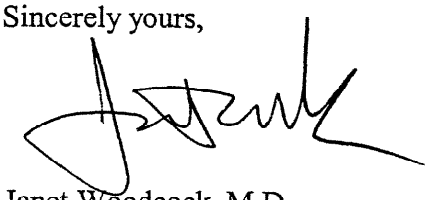
The FDA has examined the issues presented in your petition and has determined that Cortef tablets 5 mg, 10 mg, and 20 mg have a substantial share of the market for hydrocortisone tablets, and that this share represents significant sales of the drug product, in terms of both the value of those sales and the number of prescriptions filled. The Agency has further determined that it would not be in the public interest to have Cortef tablets shielded from direct generic competition. Accordingly, the FDA will designate Cortef tablets, 5 mg, 10 mg, and 20 mg (NDA 8-697), in addition to Hydrocortone tablets (NDA 8-506), as a reference listed drug in the Orange Book.

The FDA is aware that the presence of two reference listed drugs in the Orange Book creates the potential for confusion and inappropriate generic substitution. When generic hydrocortisone tablets are approved, FDA will take appropriate steps to ensure that it is made clear in the Orange Book that Cortef tablets and Hydrocortone tablets are not therapeutically equivalent to each other, and that generic drug products that are therapeutically equivalent to Cortef tablets are not therapeutically equivalent to Hydrocortone tablets and vice versa (see p. xiii of the Orange Book, 22nd ed.).

Sincerely yours,



Janet Woodcock, M.D.
Director
Center for Drug Evaluation and Research